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Profile of Mean Platelet Volume (MPV) in Patients with Nasopharyngeal Carcinoma before Undergoing Therapy in Sanglah General Hospital Denpasar

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Abstract

Introduction: Nasopharyngeal carcinoma (NPC) is a head and neck malignancy that is endemic in Southern China and Southeast Asia, including Indonesia. Currently, the TNM classification based on anatomical information is the most commonly used staging system. However, large variations were reported in clinical outcomes from one patient to another, even though they were at the same stage and had the same management strategy. MPV is an indicator of increased platelet activation and can easily be detected from peripheral blood through complete blood count analysis. MPV can be used as a marker of angiogenesis in patients with malignancy because of the role of platelets as angiogenic, metastatic and proteolytic in the inflammatory process of malignancy.
Objective: To investigate the Mean Platelet Volume (MPV) profile in Nasopharyngeal Carcinoma patients before undergoing therapy at Sanglah General Hospital, Denpasar.
Methods: This study was a cross-sectional descriptive study with 77 samples from April to June 2020 by performing a complete blood count in patients who had recently been diagnosed with nasopharyngeal carcinoma and had never undergone other treatment related to malignancy such as radiotherapy and chemotherapy.
Results: The MPV value increased the most in male group compared to the female group (87.5% : 71.4%). MPV value is also have increased the most in the age group >50 years compared to other age groups (83.6%). Clinical stage IV is known to have increased the MPV value the most compared to other clinical stage groups (100%). There was an increase in the MPV value most in the histopathological type group of NKSCC compared to the other histopathological type groups (83.7%).
Conclusion: The MPV value most increased in the male group, the age group >50 years, clinical stage IV group, and the histopathological type group of NKSCC.

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1. INTRODUCTION

Every year, malignant cancer in the head and neck area is diagnosed worldwide and is the 8th most common malignancy [1]. Nasopharyngeal carcinoma (NPC) is a head and neck malignancy that is endemic in Southern China and Southeast Asia, including Indonesia with an incidence of 50 cases per 100,000 population and a low survival rate [2].

Currently, the TNM classification (T=tumor size, N=regional node/lymph node, M=metastasis) from the American Joint Committee on Cancer (AJCC) based on anatomical information is the most commonly used staging system. However, large variations were reported in clinical outcomes from one patient to another, even though they were at the same stage and had the same management strategy. These findings indicate that the staging system is still insufficient to predict recurrence and does not reflect the biological heterogeneity of NPC patients. Although several studies have identified specific survival-related biomarkers, they are less robust and nearly unusable clinically. Thus, it is important to identify biomarkers that are effective and readily available for the prognosis of patients with malignancy [3].

Thrombosis analysis which includes platelet count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) has been carried out effectively [4]. MPV is an indicator of increased platelet activation and can easily be detected from peripheral blood through complete blood count analysis [4].

Measuring the MPV value is a simple test, cheap, useful, easy to apply, without additional costs. In addition, MPV provides information on platelet function and diameter, as well as a good indicator of platelet activation. A high MPV value indicates the presence of large and active platelets in peripheral blood vessels. In the literature, MPV is reported as a prognostic factor for several types of cancer, including head and neck malignancies [5].

MPV can be used as a marker of angiogenesis in patients with malignancy because of the role of platelets as angiogenic, metastatic and proteolytic in the inflammatory process of malignancy. Tumor cells release procoagulants, fibrinolytic factors, mediators, proteases, cytokines, which have a direct influence on platelet production and activation and directly interact with thrombosis via adhesion molecules [6].

Several reports have shown that increased MPV values are associated with the prognosis of various cancers. Cho et al., (2013) reported that patients with hepatocellular carcinoma had a higher MPV value than the control group. In addition, Kemal et al., (2014) found that patients with epithelial ovarian cancer had a significant increase in MPV values compared to the control group. Osada et al., (2010) also found that patients with gastric cancer had a higher MPV value than the control group [7].

2. MATERIALS AND METHODS

This study was a cross-sectional descriptive study by performing a complete blood count in patients who had recently been diagnosed with nasopharyngeal carcinoma and had never undergone other treatment related to malignancy such as radiotherapy and chemotherapy. The research was carried out from April 2020 to June 2020 at ENT-HNS clinic and Clinical Pathology Laboratory of Sanglah Hospital, Denpasar. This study uses consecutive sampling with 77 samples.

Patients who were newly diagnosed with nasopharyngeal carcinoma were staged to determine the clinical stage of the patient. Patients who have been erect with nasopharyngeal carcinoma at a certain stage were then asked for consent to be the study sample. Patients who were willing to be the study sample, then performed a complete blood count at the clinical pathology laboratory of Sanglah General Hospital Denpasar. Histopathological type, clinical stage and MPV data were collected in a data collection sheet. Data processing was

done by descriptive method. The data is presented in the form of tables, graphs and narratives to display the characteristics of the sample and the MPV profile of the sample.

3. RESULTS

Table 1. Characteristics of NPC Patients based on Sex

Sex	n	%
Male	56	72.7
Female	21	27.3
Total	**77**	**100**

Based on sex, the distribution of NPC patients as seen in Table 1, shows that the largest sex group of NPC patients was male, 56 samples (72.7%). While the female group was 21 samples (27.3%).

Table 2. Characteristics of NPC Patients based on Age

Age	n	%
<20 years old	0	0
20-29 years old	0	0
30-39 years old	7	9.1
40-49 years old	27	35.1
>50 years old	43	55.8
Total	**77**	**100**

Based on age, the distribution of NPC patients as seen in Table 2 shows that the largest age group of NPC patients is >50 years, 43 samples (55.8%), followed by the 40-49 age group of 27 samples (35.1%), age group 30-39 years as many as 7 people (9.1%). Meanwhile, patients with 20-29 years and age group <20 years were no samples.

Table 3. Characteristics of NPC Patients based on Clinical Staging

Clinical staging	n	%
I	0	0
II	11	14.3
III	32	41.6
IV	34	44.2
Total	**77**	**100**

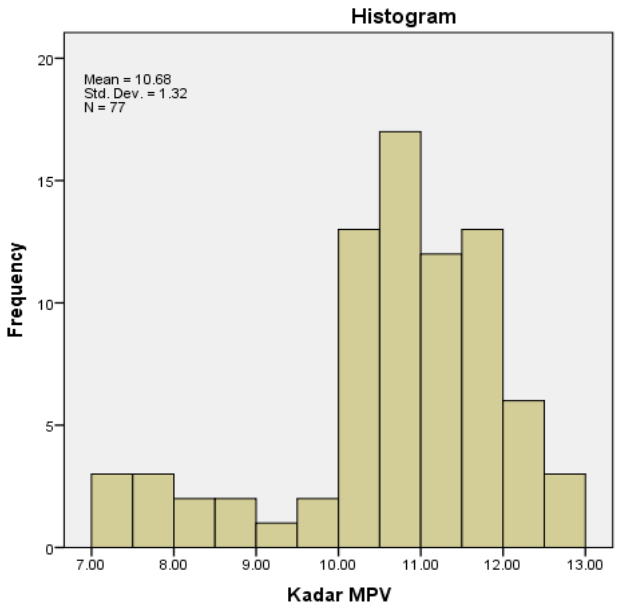
Based on the clinical stage, the distribution of NPC patients as seen in Table 3 shows that the most clinical stage group of NPC patients was stage IV as many as 34 people (44.2%), followed by the stage III group with 32 people (41.6%), the stage II group as many as 11 people (14.3%). While the stage I group was not found.

Table 4. Characteristics of NPC Patients based on Histopathological Type

Histopathological type	n	%
Keratinizing Squamous Cell Ca	0	0
Non-Keratinizing Squamous Cell	43	55.8
Undifferentiated Ca	34	44.2
Total	**77**	**100**

Based on the type of histopathology, the distribution of NPC patients as seen in Table 4 shows that the most histopathologic type group of NPC patients is non keratinizing squamous cell carcinoma as many as 43 samples (55.8%), followed by the histopathology group of undifferentiated carcinomas as many as 34 samples (44.2%). Meanwhile, the histopathological group of keratinizing squamous cell carcinoma was not found.

Further statistical analysis was conducted to determine the distribution of MPV values in NPC patients who were treated at the ENT-HNS clinic at Sanglah Hospital Denpasar according to the research variables presented in Graphic 1 and Table 5 below. Based on Graphic 1, the distribution of MPV values is mostly found in the range 10.0-12.0 fl with a mean value of 10.68±1.32.



Graphic 1. Distribution of MPV Value in NPC Patients

Table 5. Characteristics of Increase and Decrease in MPV Value in NPC Patients from Normal Value

Variable	Normal %	Increase %	Decrease %	Total
Sex				
Male	7 (1.5%)	49 (87.5%)	0 (0%)	56 (100%)
Female	6 (28.6%)	15 (71.4%)	0 (0%)	21 (100%)
Age (years)				
<20	0 (0%)	0 (0%)	0 (0%)	0 (0%)
20-29	0 (0%)	0 (0%)	0 (0%)	0 (0%)
30-39	1 (14.3%)	6 (85.7%)	0 (0%)	7 (100%)
40-49	5 (18.5%)	22 (81.4%)	0 (0%)	27 (100%)
>50	7 (19.4%)	36 (83.6%)	0 (0%)	43 (100%)
Clinical Stage				
Stadium I	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Stadium II	10 (90.9%)	1 (9.1%	0 (0%)	11 (100%)
Stadium III	3 (9.4%)	29 (90.6%)	0 (0%)	32 (100%)
Stadium IV	0 (0%)	34 (100%)	0 (0%)	34 (100%)
Histopathology				
KSCC	0 (0%)	0 (0%)	0 (0%)	0 (0%)
NKSCC	7 (16.3%)	36 (83.7%)	0 (0%)	43 (100%)
Undiff. Ca	6 (17.6%)	28 (82.6%)	0 (0%)	34 (100%)

Based on data analysis as shown in Table 5, it was found that in the male group, the MPV value increased the most compared to the female sex group. MPV value is also known to have increased the most in the age group >50 years compared to other age groups. Clinical stage IV is known to have increased the MPV value the most compared to other clinical stage groups. There was an increase in the MPV value most in the histopathological type group of NKSCC compared to the other histopathological type groups.

4. DISCUSSION

NPC is a head and neck malignancy that is endemic in southern China and Southeast Asia with an incidence of 50 cases per 100,000 population and a low survival rate for patients. In this study it was found that the sex of NPC patients with the highest frequency was male as many as 56 samples (72.3%). This result is in accordance with previous research conducted in Medan [8]. Several studies in various countries also show that there are more male NPC patients than women with an average ratio of 2–3:1.35 NPC patients are more common in male than female were reported in almost all studies, this is thought to be related to life and work habits that cause men to be frequently exposed to carcinogens that cause NPC. Workplace exposure to vapors, dust fumes and chemical gases increases the risk of NPC 2-6 times, while exposure to formaldehyde increases the risk 2-4 times.

In this study it was also seen that the age distribution of NPC patients with the highest frequency was >50 years as many as 43 people (55.8%), while in the age group 20-29 years and <20 years were not found. Although not exactly the same, it is in line with other researchers who get the most

NPC patients in the 36–60 year age group [8]. Hasibuan, et al. also found that the most age group of NPC patients was the 41-60 years group. This is because the DNA repair mechanism that has mutated (DNA repair) is not functioning properly and the body's immune system is decreased at the age of more than 40 years, so that patients with malignancy are more likely to occur in the elderly [9].

In this study it was also found that the distribution of clinical stage of NPC patients with the highest frequency was stage IV with 34 people (44.2%), while the lowest frequency was found in the stage I group of 0 people (0%) [9]. Early symptoms of NPC are not typical, similar to an upper respiratory tract infection so that they receive less attention from the patient and the examining doctor. In addition, the location of the tumor hidden in the nasopharynx so that it is difficult to examine, inadequate equipment, inadequate knowledge, trust in non-medical treatment, fear of seeing a doctor and the weak socioeconomic condition of the patients are often obstacles in making a diagnosis of this disease. Therefore, early symptoms of NPC are often missed and patients are diagnosed after the size of the tumor and enlarged lymph nodes are large at an advanced stage so that patients often come for treatment when they are at an advanced stage [9].

In this study, it was found that the distribution of histopathological types of NPC patients with the highest frequency was non keratinizing squamous cell carcinoma as many as 43 people (55.8%), while the lowest frequency was found in the histopathology group of keratinizing squamous cell carcinoma as many as 0 people (0%). This finding is the same as several studies which found that the proportion of histopathological types of NKSCC and undifferentiated carcinoma was mostly found, especially in endemic areas. Meanwhile, KSCC tends to be higher in NPC patients in non-endemic areas. Several studies reported that KSCC has an incidence rate of 25% in NPC patients in North America, but only around 1% in endemic areas, while NKSCC and undifferentiated carcinoma account for 95% of cases in high incidence areas, but around 60% in North America [10]. The incidence of NKSCC and undifferentiated carcinoma is also high in the Eskimo region, Alaska and there is also an increasing incidence in Malaysia, North Africa and Southern Europe [11]. As is known, the keratinizing type is an invasive type that has the worst prognosis because it is not radioresponsive and according to research, tobacco and alcohol play a role in its relationship to the histopathological type of keratinizing. Meanwhile, the NKSCC and undifferentiated types had a strong correlation with the predominant incidence rate at younger ages and were associated with an increase in anti-EBV antibody titers, indicating the role of the EBV virus in both types of histopathology [12].

In this study, it was proven that the MPV value in NPC patients was found to be higher in the male group of 49 (87.5%) patients compared to the female group. The prevalence of NPC tends to be more prevalent in males than females in relation to the pattern and lifestyle as well as environmental factors towards carcinogenic exposure which is more dominant in males [13].

In this study it was proven that the MPV value in NPC patients was found to be the most increased in the age group >50 years of 36 (83.6%) patients. Verdoia, et al. found that advancing age was directly related to greater mean platelet volume, but did not contribute to explaining the higher prevalence and rates of coronary artery disease in elderly patients [14].

In this study it was proven that the mean MPV value in NPC patients was found to be the most increased in stage IV of 34 (100%) patients. Sehitoglu, et al. reported that increasing the MPV value is not only important in the process of invasion and recurrence of Kaposi's sarcoma, but also important for response to therapy. They reported an increase in the MPV value in Kaposi sarcoma patients and the MPV value increased according to the stage, as well as a higher MPV value in relapsed Kaposi sarcoma patients [15]. In addition, Keles, et al. in his study of 104 renal cell carcinoma patients, he found an increase in the mean MPV value along with the higher stage of kidney cancer, where the lowest MPV mean value was found at stage I and the highest was at stage IV [16].

Evidence of the relationship between high MPV and advanced cancer is also emerging, such as colon cancer, blood cancer, kidney cancer, liver cancer, gastric cancer, and endometrial cancer. The underlying mechanism is also very clear, whereby the platelet activation process, which is stimulated by inflammatory factors such as interleukin-6, tends to produce platelets with massive and giant characteristics. Therefore, it can be expected that the number and volume of platelets will increase compared to more benign disease conditions [3].

In this study it was proven that the mean MPV value in NPC patients was found to be the most increased in the histopathological type of NKSCC, amounting to 36 (86.7%) patients. Zhang, et al. (2016) in their research suggests that the dominant histopathological type of esophageal carcinoma in some patients in China is squamous cell carcinoma, which accounts for 90% of all cases. Despite advances in radical resection and radiochemotherapy, the survival rate for people with esophageal carcinoma with squamous cell type is still low (only <30% can survive 5 years). In that study, MPV was used as a platelet activation scoring system to evaluate the prognosis of cancer patients, they evaluated the relationship between several clinical variables and overall survival and disease-free survival where it was found that MPV had the best discriminatory ability as lymph node metastasis status. The study proved that MPV biomarkers had prognostic value in 468 esophageal carcinoma patients with histopathological squamous cell type compared to undifferentiated type. Research in Korea revealed that the group of liver cancer patients with stratified squamous cell types had higher MPV levels than the normal control group.3 However, until now, there is still no literature explaining how the pathophysiological mechanism associated with increased MPV levels on the histopathological type of NKSCC.

Epithelial-mesenchymal transitions, or mesenchymal-epithelial transitions, play an important role in increased migration capacity, increased invasion capacity, increased resistance to apoptosis and increased production of extracellular matrix components. Lou, et al. showed the expression of epithelial-mesenchymal transition-related proteins, such as E-cadherin, cytokeratin (CK), vimentin and Ncadherin. Tumor cell-induced platelet aggregation triggers platelets to release alpha granules, which contain TGF-β and platelet-derived growth factor (PDGF) at concentrations several times higher than most cell types. Platelet-derived TGF-β activates the Smad signaling pathway and the trans-differentiation of circulating tumor cells into mesenchymal-like phenotypes. PDGF is a motor of epithelial transition that contributes to cancer invasion and angiogenesis. In addition, TGF-β was shown to increase the expression of PDGF and PDGF receptors through β catenin activation and signal transducer and activator of transcription 3 (STAT3) [17].

5. CONCLUSION

This study found that the MPV value most increased in the male group, the age group >50 years, clinical stage IV group, and the histopathological type group of NKSCC.

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